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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/024,988	02/17/98	NELSON	R 5015C1

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HM22/0522

EXAMINER

UNGAR, S

ART UNIT

PAPER NUMBER

1642

DATE MAILED:

05/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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1. The Amendment filed March 6, 2000 (Paper No. 8) in response to the Office Action of September 22, 1999 (Paper No. 5) is acknowledged and has been entered. Previously pending claim 31 has been amended. Claims 31, 33, 40 and 41 are currently being examined.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration submitted on March 6, 2000, Paper No. 6) is defective because only Inventor Krone is listed on the declaration. It appears that Applicant is changing the inventive entity, however, no Request to Change Inventorship has been received. If the inventive entity is not being changed, a new declaration, signed by all of the Inventors is required. If the inventive entity is being changed Applicant must submit a petition under 37 CFR 1.48(a) for Change of Inventorship.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. Claims 40 and 41 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 40 and 41 are indefinite because claim 40 recites the phrase "a known or equal amount". The claims are confusing because it is not clear what the "equal amount" is equal to.

Claims 31, 33, 40 and 41 are indefinite because claim appears to be missing an essential method step. Section 31 c) recites "quantifying said analyte" but does not require quantifying the IRS. It is not clear how a ratio of analyte signal to IRS signal can be made without quantifying the IRS, further, it is not clear from step 31 b) that the IRS is either captured or isolated.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions

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covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

6. Claims 31, 33, 40, 41 are rejected under 35 U.S.C. § 103 as being unpatentable over van Ginkel et al, of record, in view of US Patent No. 5,707,799 or US Patent No. 4,743,561.

The claims are drawn to a method for quantifying an analyte in a specimen comprising combining an internal reference species (IRS) in a known concentration to calibrate all subsequent steps with the analyte in the specimen, capturing and isolating said analyte by combining the IRS-containing solution with an affinity reagent, quantifying said analyte using mass spectrometric analysis to resolve distinct signals for said analyte and said IRS to determine the ratio of the analyte signal to the IRS signal wherein said quantifying step further comprises using working curve analysis which comprises first obtaining a mass spectrum of a first portion of said IRS containing specimen then making a plurality of standard preparations each containing a known but differing amount of said analyte and each containing a known or equal amount of said IRS, then obtaining respective mass spectra of each whereby said respective mass spectra provide a working curve relationship of mass spectra relative to analyte concentration and then using said first mass spectrum and the standard preparation mass spectra working curve relationship to quantify said analyte.

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Van Ginkel et al teach a method for quantifying an analyte in a specimen comprising capturing and isolating an analyte by combining it with an affinity reagent (p. 556, col 2) combining an IRS, an isotopically labeled internal standard for quantification and quality control (p. 555, col 1) in a known concentration with the captured and isolated analyte to calibrate all subsequent steps with the analyte in the specimen (p. P. 556, col 1), wherein the processed specimen is analyzed by mass spectrometric analysis which resolves distinct signals for the analyte and for the IRS (p. 556, col 2) wherein the quantification of the analyte is determined by the ratio of the analyte to the internal standard (that is the first mass spectrum of a first portion of the IRS containing specimen) and the quantification procedure used includes a linear calibration curve which is fitted with the ratio of abundance of the ions in question (i.e. tert-butyl-beta-agonists/internal standards) as the independent variable and the concentration of standard (ng/injection vial) as the dependent variable which procedure yields linear calibration curves with an intercept not significantly different than zero (pl 556, col 2) which inherently requires a plurality of standard preparations each containing a known but differing amount of said analyte and each containing a known or equal amount of said IRS to produce said linear calibration curve.

Van Ginkel et al teach as set forth above but do not teach a method wherein the specimen is combined with an internal reference species of known concentration prior to the capturing and isolating step wherein both the analyte and the IRS are captured and isolated.

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US Patent No. 5,707,799 teach a method for quantitative determination of analytes in test samples comprising the steps of using a control means to verify an assay result wherein the test sample containing the analyte is contacted with a predetermined amount of labeled reagent to form a mixture containing an analyte/labelled reagent complex, the resulting mixture contacts a capture site containing an immobilized anti-analyte specific binding member that binds the analyte/labelled reagent complex which is the test sample capture site and teach that the complex can be used to establish a positive control ((col 13, line 54 to col 14, line 31).

The teaching of US Patent No. 4,743,561, although drawn specifically to fluorometric assays is clearly applicable to the instant rejection. US Patent No. 4,743,561 teaches that it is well recognized that in order to maximize the sensitivity and specificity of an assay, inhibiting and interfering factors must be compensated for by using an internal standard whereby the standard is added to an aliquot of sample and the entire assay procedure is carried out using the aliquot containing the internal standard (col 2, lines 50-59).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the methods of Van Ginkel et al and the methods of US Patent No. 5,707,799 or US Patent No. 4,743,561 in order to produce an assay method wherein a standard was included in the immunoisolation step of van Ginkel et al because US Patent No. 5,707,799 clearly teaches that inclusion of a standard labeled reagent is useful for establishing a positive control and because US Patent No. 4,743,561 teaches that it is well recognized that internal

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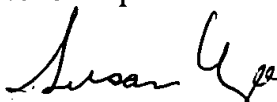
standards are useful for maximizing sensitivity and specificity of an assay. One of ordinary skill in the art would have been motivated to provide an internal standard in the analyte mix because US Patent No. 4,743,561 specifically teaches that inhibiting and interfering factors must be compensated for by using an internal standard in the assay aliquot.

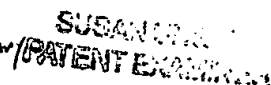
7. All other objections and rejections imposed in Paper No. 5 are withdrawn.
8. No claims allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.


Susan Ungar



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Primary Patent Examiner

May 17, 2000